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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/075,918	02/13/2002	Nicole Chantel Barvian	A0000426-01-CFP	9234

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EXAMINER	
OH, TAYLOR V	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 04/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/075,918	BARVIAN ET AL.	
	Examiner	Art Unit	
	Taylor Victor Oh	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3, 5-10, and 13-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-10 and 13-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/22/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicant's arguments with respect to claims 1-3, 5-10 and 13-17 have been considered but are moot in view of the new ground(s) of rejection.

The Status of Claims:

Claims 1-3, 5-10 and 13-17 are pending.

Claims 1-3, 5-10 and 13-17 have been considered.

Claims 4, 11, and 12 have been canceled.

DETAILED ACTION

1. Claims 1-3, 5-7, and 10 and 13-17 are under consideration in this Office Action.

Priority

2. Provisional Patent Application number 60/268,736 filed 2/14/2001 has been acknowledged.

Drawings

3. None.

Claim Objections

The amendment filed 1/22/2004 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

Claims 1-2 and 5 have been amended to introduce the phrase " wherein the compound isophthalic acid is bis-(1,3-benzodioxol-5-ylmethyl)ester is excluded" which is different than the original specification as filed. A close inspection of the original claims and specification do not provide antecedent basis for the proposed changes. New matter can not be introduced into specification at any time during the prosecution, unless there is a supporting description that would support the proposed changes. Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2 and 5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In claims 1-2 and 5, the phrase " wherein the compound isophthalic acid is bis-(1,3-benzodioxol-5-ylmethyl)ester is excluded" has been introduced, which is different than the original specification as filed. A close inspection of the original claims and specification do not provide antecedent basis for the proposed changes. New matter

can not be introduced into specification at any time during the prosecution, unless there is a supporting description that would support the proposed changes. Applicant is required to cancel the new matter in the reply to this Office Action.

Claims 1-3 , 5-6, 8-10, and 13-17 are rejected under 35 U.S.C. 112, first paragraph. , because the specification, while being enabling for inhibiting matrix metalloproteinase enzymes ,such as MMP-13 in an animal by administering to the mammal the compound of formula I for any known disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are directed to not the specific diseases, but all kinds of the diseases by using the mechanistic nature of inhibiting matrix metalloproteinase enzymes. The specification falls short because data essential for treating many diseases by means of inhibiting matrix metalloproteinase enzymes is not described in the specification.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The Nature of the Invention

The nature of the invention in claims 1-3 , 5-6 , and 10 is the inhibiting matrix metalloproteinase enzymes ,such as MMP-13 in an animal by administering to the mammal the compound of formulas I-III, and V-VI, thereby treating numerous diseases, for example, breast carcinoma, rheumatoid arthritis, osteoarthritis, inflammation, a heart failure, and etc.

The State of the Prior Art

The state of the prior art is that according to US Patent No. 5,948,780, MMP inhibitors have been used to prevent and treat congestive heart failure and other cardiovascular diseases. Recent data has revealed that specific enzymes are closely related to some diseases ,while there is no effect on other diseases. The MMPs are generally classified based on their substrate specificity; particularly , the collagenase subfamily of MMP-1, MMP-8, and MMP-13 selectively cleave interstitial collagen tissue. This has been noticed by the discovery that only MMP-13 is over expressed in breast carcinoma, whereas MMP-1 alone is over expressed in papillary carcinoma (see Chen et al., J. Am .Chem. Soc., 2000;122;9648-9654). Furthermore, according to Wo/01/63244A1 and US Patent No. 6,008,243 few selective inhibitors of MMP-13 have been approved: however, no selective or nonselective inhibitor of MMP-13 has been approved for treating any disease in any animal.

The predictability or lack thereof in the art

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that inhibiting the MMPs would result in only the specific site of the interstitial collagen tissue; this kind of treatment can not translated to all the possible treatment of any disease in regards to their therapeutic effects.

Hence, in the absence of a showing of correlation between all the diseases claimed as capable of treatment by the compounds of formulas I-III, and V-VI and the inhibition of matrix metalloproteinase, one of skill in the art is unable to fully predict possible results from the administration of the claimed compounds of formulas I-III, and V-VI due to the unpredictability of the role of inhibiting the MMPs, i.e. whether promotion or inhibition would be beneficial for the treatment of the diseases.

The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The amount of direction or guidance present

The direction present in the instant specification is that the compounds of formulas I-III, and V-VI can inhibit the the MMPs which helps in the treatment for congestive heart failure , breast carcinoma, and papillary carcinoma. However, the specification is silent and fails to provide guidance as to whether the diseases listed (pages 53 and 55) require the inhibition of the MMPs for treatment, i.e. the specification fails to provide a correlation between the diseases listed and the inhibition of the MMPs. Also, there is no direction and guidance for the inhibition of the MMPs for the treatment of any kinds of diseases.

The presence or absence of working examples

There is no working example for the treatment of breast carcinoma, rheumatoid arthritis, osteoarthritis, inflammation, or a heart failure. Furthermore, there are not other working examples for any other diseases listed in the specification. Also, the compounds which are discloses in the specification have no pharmacological data regarding the treatment of any other disease besides inhibitory activity of various MMPs using compounds from various classes and have no data on the possible treatment of the various diseases that require the inhibitory activity of various MMPs. Also, the specification fails to provide working examples as to how the listed diseases can be treated by the inhibition of various MMPs, i.e. again, there is no correlation between the diseases listed and inhibition of various MMPs.

The breadth of the claims

The breadth of the claims is that the compounds of formulas I-III, and V-VI can treat any disease by the inhibition of the MMPs , without regards as to the affect of the inhibition of the MMPs on the stated diseases.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what listed diseases would be benefited by the inhibition of the MMPs and would furthermore then have to determine whether the claimed compounds would provide treatment of the disease by the inhibition of the MMPs.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compounds of formulas I-III, and V-VI for the treatment of any disease by the inhibition of the MMPs. As a result, necessitating one of skill to perform an exhaustive search for which diseases can be treated by the compounds of formulas I-III, and V-VI in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, and 5 are rejected under 35 U.S.C. 102(b) as being anticipated clearly by (JP-405193260).

Japanese patent (405193260) discloses an isophthalic acid bis-(1,3-benzodioxo-5-ylmethyl) ester compound (see page 3, compound # 0013).

This is identical with the claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taylor Victor Oh whose telephone number is 571-272-0689. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Mckane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

*** 4/17/09

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PRIMARY EXAMINER
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